

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1-22. (cancelled)

23. (currently amended) A modified therapeutic polypeptide having a modification only in an immunodominant epitope of the unmodified therapeutic polypeptide, wherein the immunodominant epitope is an epitope that is recognized by an antibody or population of antibodies obtained from a naive human or animal or population thereof,

wherein the modification reduces ~~the~~ an immune response to the polypeptide compared to the unmodified therapeutic polypeptide while retaining a substantial therapeutic activity of the unmodified therapeutic polypeptide,

wherein the modification is a deletion, substitution, or chemical modification of at least one amino acid in the immunodominant epitope.

24. (cancelled)

25. (currently amended) A modified human recombinant thrombopoietin ~~comprising~~ consisting of ~~[[an]]~~ the amino acid sequence of amino acids 22 to 338 of SEQ ID NO:13.

26. (withdrawn and currently amended) A modified therapeutic polypeptide according to claim 23, wherein the polypeptide is human recombinant thrombopoietin with at least one modification of amino acids of SEQ ID NO:2 ~~312 to 332~~ (SEQ ID NO:2).

27. (withdrawn and currently amended) A modified therapeutic polypeptide according to claim 26, wherein the modification is in amino acids of SEQ ID NO:1 ~~318 to 332~~ (SEQ ID NO:1).

28. (cancelled)

29. (withdrawn and currently amended) A modified therapeutic polypeptide according to claim 23, ~~wherein the modification is a chemical modification of at least one amino acid in the immunodominant epitope,~~ wherein the chemical modification is N-glycosylation or pegylation.

30. (currently amended) A method of modifying a nucleic acid encoding a ~~modified~~ therapeutic polypeptide comprising:

- a) identifying at least one immunodominant epitope in the therapeutic polypeptide, by contacting the therapeutic polypeptide or fragments thereof with an antibody or population of antibodies obtained from a naive human or animal or population thereof;
- b) providing an isolated nucleic acid sequence encoding the therapeutic polypeptide; and
- c) modifying the isolated nucleic acid to encode a modified therapeutic polypeptide wherein the modified polypeptide has at least one change in the immunodominant epitope and wherein the change reduces an immune response compared to the unmodified therapeutic polypeptide while still retaining a substantial therapeutic activity of the therapeutic polypeptide.

31. (cancelled)

32. (withdrawn and currently amended) An isolated nucleic acid encoding a modified human thrombopoietin whereby the modified thrombopoietin has a modification only of amino acids of SEQ ID NO:2 312 to 332 (SEQ ID NO:2), wherein the modification is a deletion or substitution of at least one amino acid.

33. (currently amended) A pharmaceutical composition comprising the modified therapeutic polypeptide of claim 23 and a pharmaceutically acceptable carrier.

34. (withdrawn and currently amended) A method of treating thrombocytopenia by administering a modified recombinant human thrombopoietin, wherein the human recombinant thrombopoietin has at least one modification only of amino acids of SEQ ID NO:2 312-332 (~~SEQ ID NO:2~~), wherein the modification reduces an immune response to human thrombopoietin while still retaining a substantial therapeutic activity of human thrombopoietin, wherein the modification is a deletion, substitution, or chemical modification of at least one amino acid.

35. (currently amended) A modified native thrombopoietin comprising at least one ~~a~~ modification ~~in an immunodominant epitope~~ only of amino acids of SEQ ID NO:2 of native thrombopoietin, wherein the modification reduces the immune response to thrombopoietin while retaining a substantial therapeutic activity of thrombopoietin, wherein the modification is a deletion, substitution, or chemical modification of at least one amino acid.

36. (cancelled)

37. (withdrawn and currently amended) The modified thrombopoietin of claim 35, wherein the epitope has an amino acid sequence of amino acids of SEQ ID NO:1 318 to 332 of native thrombopoietin (~~SEQ ID NO:1~~).

38. (previously presented) The modified thrombopoietin of claim 35, wherein the modification comprises a deletion of one or more of the amino acids of the immunodominant epitope.

39. (currently amended) The modified thrombopoietin of claim 38, wherein the modification consists of ~~a deleting~~ a deletion of the amino acid sequence of SEQ ID NO: 1.

40. (withdrawn and currently amended) The modified thrombopoietin of claim 35 ~~36~~, wherein the modification comprises an amino acid substitution of an amino acid in the immunodominant epitope.

41. (cancelled)

42. (withdrawn and currently amended) The modified thrombopoietin of claim 35 ~~36~~, wherein the chemical modification comprises N-glycosylation or N-pegylation of at least one amino acid in the immunodominant epitope.

43. (previously presented) A composition comprising a modified thrombopoietin of claim 35 and a physiologically acceptable carrier.

44. (currently amended) An isolated nucleic acid comprising a modified nucleic acid sequence that encodes ~~encoding~~ a modified thrombopoietin according to claim 35, wherein the modification is a deletion or a substitution.

45. (previously presented) A vector comprising an isolated nucleic acid of claim 44.

46. (previously presented) A host cell comprising a vector of claim 45.

47. (previously presented) A method for producing a modified thrombopoietin comprising culturing a host cell of claim 46 under conditions suitable for production of a modified thrombopoietin, and recovering the modified thrombopoietin from the cell culture.

48. (previously presented) A method of treating thrombocytopenia comprising administering an effective amount of a modified thrombopoietin of claim 35 to a subject.

49. (new) The method of treating thrombocytopenia of claim 34, wherein the chemical modification comprises N-glycosylation or N-pegylation of at least one amino acid in the immunodominant epitope.

50. (new) A fusion polypeptide comprising a modified human recombinant thrombopoietin consisting of the amino acid sequence of amino acids 22 to 338 of SEQ ID NO:13.

51. (new) A modified therapeutic polypeptide having a modification only in an immunodominant epitope of the unmodified therapeutic polypeptide, prepared by the process comprising:

a) identifying at least one immunodominant epitope in the unmodified therapeutic polypeptide that has at least one substantial therapeutic activity, wherein the immunodominant epitope is identified by binding of the epitope to an antibody or population of antibodies obtained from a naive human or animal or population thereof; and

b) modifying the immunodominant epitope to reduce an immune response while retaining a substantial therapeutic activity of the unmodified therapeutic polypeptide, wherein the modification is a deletion, substitution, or chemical modification of at least one amino acid in the immunodominant epitope.